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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/671,387	09/25/2003	Neil H. Bander	10448-183004	4249

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EXAMINER	
CANELLA, KAREN A	

ART UNIT	PAPER NUMBER
1643	

DATE MAILED: 06/06/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/671,387	BANDER	
	Examiner	Art Unit	
	Karen A. Canella	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-16 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-16 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 7/22/04; 12/19/05
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-16 are pending and examined on the merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The instant method claims are reliant upon the identity of antibodies or antigen-binding fragments thereof, wherein said antibodies bind to the antigen bound by HB11892. When given the broadest reasonable interpretation, the claims are not limited to antibodies which bind the same epitope as HB11892, but also include antibodies which bind the same antigen as HB11892 at different epitopes. The instant specification has described the cloning and the screening of the antibody C37 which is the antibody deposited as HB11892. The specification teaches that said antibody specifically binds to the prostate tumor cell line LNCaP (page 43, lines 9-10). The specification provides no further description of the antigen comprising the epitope to which C37 binds. The description of the C37 antibody does not provide an adequate written description of the antigen to which C37 binds because said antigen can have numerous epitopes and a description of an antibody which binds to one of said epitopes does not provide a nexus to other antibodies which binds to alternative epitopes on said antigen. It is noted that the written description guidelines provides for antibodies which bind to a fully characterized protein. In the instant case, the antigen which is on the surface of LNCap cells and bound by the HB11892 is not fully characterized. Therefor antibodies which bind to said antigen beyond that of C37 deposited as HB1111892 are also not adequately characterized and do not meet the written description requirement of 112, 1st paragraph.

Claims 1-16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. the instant claims require the deposited antibody HB11892 for practice of the claimed method. .The recitation of the ATCC deposit number on page 14 of the specification provides insufficient assurance that all required deposits have been made and all the conditions of 37 CFR 1.801-1.809 have been met.

If the deposits is made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by applicant or assignees or a statement by an attorney or record who has the authority and control over the conditions of deposit over his/her signature or registration number stating that the deposit has been accepted by an International Depository authority under the provisions of the Budapest Treaty, that all restrictions upon public access to the deposits will be irrevocably removed upon the grant of a patent on this application and that the deposit will be replaced if viable samples cannot be dispensed from the depository as required. This requirement is necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves this specific matter to the discretion of each State.

If the deposit is not made under the provisions of the Budapest Treaty, then in order to certify that the deposits comply with the criteria set forth in 37 CRF 1.801-1.809 regarding availability and permanency of deposits, assurance of compliance is required. Such assurance may be in the form of an affidavit or declaration by applicants or assignees or in the form of a statement by an attorney of record who has the authority and control over the conditions of deposit over his/her signature and registration number averring:

(a) during the pendency of this application, access to the deposits will be afforded to the Commissioner upon request:

(b) all restrictions upon the availability to the public of the deposited biological material will be irrevocably removed upon the granting of a patent on this application:

( ) the deposits will be maintained in a public depository for a period of at least thirty years from the date of the deposit or for the enforceable life of the patent or for a period of five

years after the date of the most recent request for the furnishing of a sample of the deposited biological material, whichever is longest; and

(d) the deposits will be replaced should they become non-viable or non-replicable.

Amendment of the specification to recite the date of deposit and the complete name and address of the depository is required. As an additional means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

If deposits are made after the effective filing date of the application for patent in the United States, a verified statement is required from a person in a position to corroborate that the deposited hybridomas are producing the antibody of C37 as described in the specification as filed and are the same as those deposited in the depository, stating that the deposited hybridomas are producing identical antibody as described in the specification and were in the applicant's possession at the time the application was filed.

Applicant's attention is directed to In re: Lundak, 773 F. 2d.1216, 227 USPQ 90 (CAFC 1985) and 37 CRF 1.801-1.809 for further information concerning deposit practice.

Claims 1-16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating prostate cancer or a method of delaying the progression of prostate cancer, does not reasonably provide enablement for a method of preventing prostate cancer or a method of delaying the development of prostate cancer. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The instant methods are drawn in part to prophylactic treatment of individuals with an antibody which binds to an antigen expressed on the surface of prostate epithelial cells such that prostate cancer is prevented or the development of prostate cancer is delayed.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue

experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The specification does not provide any teachings of the prophylaxis of prostate cancer, how to determine the individuals who will develop a particular cancer, nor how to effectively prevent prostate cancer before occurrence.

The specification fails to provide objective evidence that the antigen to which HB11892 binds is present on pre-malignant prostate cells and can be used as target to eliminate said cells before they become malignant. Thus, one of skill in the art would not be able to use the method of the invention without undertaking to determine how to select for individuals which will develop prostate cancer and determining the optimum time before the development of a malignant prostate cells at which to administer the antibody conjugate of the invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 4, 5, 8, 10, 14 are rejected under 35 U.S.C. 102(b) as being anticipated by Deguchi et al (Cancer Research, 1986, Vol. 46, pp. 3751-3755).

Claim 1 is drawn in part to a method of treating prostate cancer comprising administering an antibody which binds to an antigen expressed on the surface of prostate epithelial cells, said

antigen including the epitope bound by the antibody of deposit number HB11892, wherein the antibody is an IgG which binds to viable cells and wherein the antibody is conjugated to a cytotoxic drug. Claim 4 embodies the method of claim 1 wherein the administration is parenteral. Claim 5 embodies the method of claim 4 wherein the administration is intravenous. Claim 8 embodies the method of claim 1 wherein the antibody is a monoclonal antibody. Claim 10 embodies the method of claim 1 wherein the cytotoxic drug is selected from a group including a therapeutic drug. Claim 14 embodies the method of claim 1 wherein the antibody is in a composition with a pharmaceutically acceptable carrier.

Deguchi et al teach the administration of a conjugate comprising methotrexate and a monoclonal IgG which is specific for human prostatic acid phosphatase to mice carrying prostate tumor LNCap cells ((page 3751, second column, under the headings of "Mice and Cell Lines") and page 3754, first column, under the heading "Preliminary Study on Antitumor Activity of the Conjugate in Vivo").

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-5, 7, 8, 10, 11, 14-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bander (Seminars in Oncology, 1994, Vol. 21, pp. 607-612, reference of the IDS submitted Dec 19, 2005) in view of Israeli et al (Cancer Research, 1994, Vol. 54, pp. 1807-1811).

Claim 2 embodies the method of claim 1 wherein the prostate cancer is metastatic. Claim 3 embodies the method of claim 2 wherein the metastasis involves bone marrow or lymph nodes. Claim 7 embodies the method of claim 1 wherein the antibody is administered following prostatectomy. Claim 11 embodies the method of claim 1 wherein the cytotoxin is a compound emitting radiation. Claim 15 embodies the method of claim 1 wherein the antibody is

administered in conjunction with a second therapeutic modality. Claim 16 embodies the method of claim 15 wherein the second modality is selected from surgery, radiation, chemotherapy, immunotherapy or hormone replacement.

Bander et al teach that prostate cancer is a relatively radiosensitive target and that monoclonal antibodies can by linked with therapeutic radioisotopes to precisely target tumor sites while sparing normal tissues; Bander suggests that that MoAb based therapy can be utilized in an adjuvant setting, thus fulfilling the specific embodiment of another therapeutic modality (page 607, second column, line 13 to page 608, second column, line 5). Bander et al teach that prostate cancer metastasizes predominately to the bone marrow and lymph nodes which are conducive to receive high levels of therapeutic antibody. Bander does not specifically teach a monoclonal antibody which would bind to the antigen which binds the deposited antibody.

Israeli et al teach antibodies which bind to the LNCap cell line (page 1808, second column, under the heading "Immunohistochemical Detection of PSM"). The specification teaches that the deposited antibody binds to LNCap cells. Israeli et al teach that the antibody which binds to PSM provides an attractive cell surface epitope for antibody-directed cytotoxic targeting modalities (page 1810, first column, lines 12-14).

It would have been prima facie obvious at the time the claimed invention was made to use the antibody of Israeli et al for the treatment of metastatic prostate cancer as suggested by Bander. One of skill in the art would have been motivated by the suggestion of Israeli et al to target the PSM protein bound by the 7E11-C5.3 antibody to target cytotoxic agents to prostate cancer cells. One of skill in the art would have been motivated to treat metastatic cancer as residual disease after a prostatectomy.

Claims 1-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bander and Israeli et al as applied to claims 1-8, 10, 11, 13-16 above, and further in view of Schlom ('Monoclonal Antibodies: They're More and Less Than You Think', In" Molecular Foundations of Oncology, 1991, Broder, Ed. pp. 95-134, reference of the IDS submitted July 22, 2004).

The combination of Bander and Israeli et al render obvious the specific limitations of claims requiring a therapeutic radionuclide conjugated to the antibody of Israeli et al, wherein said conjugate is administered intravenously. The combination of prior art reference does not

specifically teach the administration of an antibody conjugated to a cytotoxic agent derived from a plant, the administration of antibody fragments or intracavity administration.

.Claim 6 embodies the method of claim 1 wherein the administration is intracavitary.

Claim 9 embodies the method of claim 1 wherein the antigen binding portion of the antibody is selected from a Fab fragment, a F(ab')2 fragment and a Fv fragment.

Claim 13 embodies the method of claim 1 wherein the cytotoxic drug is a molecule of plant origin.

Schlom teaches the use of antibody conjugates with ricin for the specific targeting of the toxin ricin moiety which fulfills the specific embodiment of molecule of plant origin (page 108, first column). Schlom teaches the advantages of using antibody fragments versus whole antibodies in that the fragments more easily penetrate the vasculature of the targeted tumor (page 119, second column). Schlom also teaches intracavity administration of monoclonal antibodies can be more efficient that intravenous administration (page 101).

It would have been prima facie obvious at the time the claimed invention was made to administer the antibody of Israeli et al conjugated to either the therapeutic radioisotope or ricin by means of intracavity administration. It would also have been obvious to use an antigen-binding fragment of the antibodies such as the F(ab')2 fragment as the conjugate in order to enable more efficient penetration into the tumor vasculature and more accumulation of the cytotoxic moiety in the tumor cells.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A. Canella whose telephone number is (571)272-0828. The examiner can normally be reached on 11 am to 10 pm, except Wed, Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571)272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Karen A. Canella, Ph.D.
5/30/2006

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